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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,870	05/04/2001	Chung K. Chu	G25-063	1452

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,870	CHU ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 24-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 24-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, wherein the azide group occurs in place of an amino moiety (Species 1) and wherein the azide derivative is a purine (Species 2), in Paper No. 9 dated March 11, 2003, is acknowledged.

Applicant's Response dated February 2, 2004

2. In the Response filed February 2, 2004, claim 1 was amended; claims 2-23 were canceled; and claims 24-31 were added.

3. Claims 1 and 24-31 are pending. An action on the merits of claims 1 and 24-31 is contained herein below.

4. The rejection of claims 1, 7, and 13 under 35 U.S.C. 112, second paragraph, has been rendered moot in view of applicant's amendment dated February 2, 2004.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall' set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 24-29, and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition of an azide derivative of a biologically active therapeutic purine nucleoside or purine nucleotide wherein said

azide group occurs at the 6-position on the purine base of said purine nucleoside or nucleotide in place of an amino moiety, does not reasonably provide enablement for 1) azide derivatives wherein the azide moiety is not at the 6-positon of the purine base or 2) azide derivatives wherein the moiety at the 9-position of the purine ring is not a nucleoside or nucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make and use the invention as of its filing date, *In re Glass*, 181 USPQ 31; 492 F2.d 1228 (CCPA 1974).

The instant specification invites the skilled artisan to experiment. The factors which must be considered in determining undue experimentation are set forth in *In re Wands*, 8 USPQ2d 1400. The factors include: 1) quantity of experimentation necessary, 2) the amount of guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the predictability of the art, and 7) the breadth of the claims.

The instant specification is drawn to azide derivatives of pharmaceutically active compounds. Azide derivatives of the instant invention lack support wherein applicants fail to provide a written description which teaches how to make said azide derivatives. While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and

techniques where necessary, as to enable those persons skilled in the art to make and utilize the invention. A broad claim requires a correlatively broad and sufficient disclosure to support it. Presently, the examples in the instant specification are limited to the preparation of the azide derivative of cordycepin, FAAddP and FMAddA (2'-F-ara-ddI azide prodrugs) and respective biological activities. Applicants do not provide an adequate written description which provides guidance for the preparation of azide derivatives of purine compounds wherein the azide moiety is not at the 6-position. Applicants do not provide an adequate written description which provides guidance for the preparation of azide derivatives wherein the moiety at the 9-position of the purine base is not a nucleoside or nucleotide; more specifically, applicants do not teach the preparation of compounds wherein a dioxolane moiety is at the 9-position of the purine base. Additionally, enzymes are very selective in terms of activity. One of ordinary skill in the art would not predict that a specific enzyme or class of enzymes would convert azide derivatives as broadly claimed into their respective active forms. Examples and description should be of sufficient scope as to justify the scope of the claims. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula. A disclosure involving a new chemical compound or composition must teach persons skilled in the art how to make the compound. The process is considered to be incomplete wherein applicants set forth the preparation of compounds wherein various moieties are left undefined in full, clear and exact terms.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The variable R^2 reads upon a "dangling valence" when R^2 is O. The incorporation of said "dangling valence" renders claims 29-31 indefinite as it is seen to affect the effective character of the nucleus.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1 and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Bauman et al. U.S. 5,180,824 (Bauman).

Bauman discloses the utilization of 6-azido-2-fluorpurine as an intermediate for the synthesis of fludarabine, fludarabine phosphate and related nucleoside pharmacological agents (Abstract). Bauman's disclosure of 6-azido-2-fluorpurine (compound 3) and its corresponding nucleoside (compound 5) anticipates the instantly claimed purine compounds (columns 3-4). Bauman further discloses the reduction of the azide to an amine.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 1 and 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauman et al. U.S. 5,180,824 (Bauman) in combination with Gmeiner et al. US 5,457,187 (Gmeiner).

Claims 1 and 24-28 are drawn to a pharmaceutical composition comprising an azide derivative of a biologically active therapeutic purine nucleoside, purine nucleotide or other purine compound wherein said azide group occurs on the purine base in place of an amino moiety.

Bauman teaches the utilization of 6-azido-2-fluorpurine as an intermediate for the synthesis of fludarabine, fludarabine phosphate and related nucleoside pharmacological agents (Abstract). Bauman's teaching of 6-azido-2-fluorpurine (compound 3) and its corresponding nucleoside (compound 5) are embraced by the instantly claimed purine compounds (columns 3-4). Bauman further teaches the reduction of the azide to an amine.

Bauman differs from the instantly claimed invention in that Bauman does not explicitly teach azido-containing purine nucleotides; however, the conversion of the nucleoside compound into the corresponding nucleotide is routine in the art and seen to be well within the purview of one of ordinary skill in the art at the time of the invention.

Gmeiner teaches the delivery of nucleosides as homo-oligomeric nucleotides confers several distinct advantages relative to their delivery as nucleoside bases, nucleosides, or analogues resulting in a significant reduction of the dose required for a positive biological response and a reduction of dose-dependent toxic side-effects (column 3, lines 7-32).

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ the azido-nucleoside derivatives of Bauman as their corresponding nucleotides or oligonucleotides as Gmeiner teaches that there are several advantages

for doing so. Based on the teachings of Gmeiner, one of ordinary skill in the art at the time of the invention would have sufficient motivation and a reasonable expectation of success in converting the nucleoside compounds of Bauman into their corresponding nucleotides.

Conclusion

15. Claims 1 and 24-31 are pending. Claims 1 and 24-31 are rejected. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Examiner
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April 14, 2004